REMARKS

Claims 1-6, 8-19, and 21-28 were pending prior to this Response. By the present communcation, no claims have been added or cancelled and claims 1, 3, 21, 23, 24, 26, 27 and 28 have been amended to define Applicants' invention with greater particularity. The claim amendments add no new matter, being fully supported by the Specification and original claims. Accordingly, claims 1-6, 8-19 and 21-18 are currently pending and under consideration in this application.

The Drawings

The Office Action indicates that the drawing corrections previously submitted are approved and requests filing of formal drawings with this Response. Accordingly, attached is Exhibit A containing formal drawings for the Figures of the application.

The Objection to Claim 26

Claim 26 is objected to for allegedly containing an informality. The Examiner asserts that the subject matter of 26 is unrelated to the subject matter of 25, from which it depends. To overcome any informality, claim 26 has been amended to be dependent upon claim 24, as suggested by the Examiner. Accordingly, reconsideration and withdrawal of the objection are respectfully requested.

The Rejection under 35 U.S.C. § 102(e)

Applicant respectfully traverses the rejection of claims 1-5, 8-18, and 24-26 as allegedly being anticipated under 35 U.S.C. § 102(e) over Thompson et al. (U.S. Patent No. 6,329,851; hereinafter " the '485 patent").

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration (In re Spada, 15 USPQ 2d 1655 (Fed. Cir. 1990), In re Bond, 15 USPQ 2d 1566 (Fed. Cir., 1990). Applicant's invention methods for identifying an enzymatic activity of interest, as defined by amended claim 1, distinguish over the disclosure of Thompson by requiring:

co-encapsulating in a micro-environment selected from a liposome, bead, cell, ghost red blood cell and ghost macrophage an environmental library comprising a mixture of target DNA obtained from a mixed population of organisms with a mixture of DNA probes comprising a detectable label and at least a portion of a DNA sequence encoding at least one enzyme having a specified activity; incubating the co-encapsulated mixture under such conditions and for such time as to allow hybridization of complementary sequences in the co-encapsulated mixture; and screening the micro-environment to recover the hybridized complementary sequences containing the detectable label, thereby enriching the DNA sequences containing the at least partial coding region for the specified activity in the recovered target DNA. The methods of amended claims 27 and 28 also contain these limitations or slight variations thereof.

Thus, Applicants' presently claimed invention, as defined by amended claim 1, 27 and 28 is not the purposeful creation of novel activities or pathways by combinatorial techniques, but rather expression cloning of DNA derived from a mixture of uncultivated organisms to produce libraries that contain naturally occurring activities or gene clusters or pathways or genes as found in nature, without manipulation to create a combinatorial library. It can be envisioned that once Applicants have cloned DNA producing such activities or pathways as they occur naturally in organisms in the environment, such molecules could be further manipulated by substituting genes or portions thereof from other species or strains using combinatorial methods. Thus,

Applicants reiterate that the claimed invention is not directed to a "combinatorial library," but rather recites screening environmental libraries containing sequences that are naturally occurring and which have not been rearranged or recombined in a laboratory setting for the purpose of creating new, combinatorially produced, pathways.

By contrast, Applicants respectfully submit that the '485 patent fails to describe each and every element of Applicant's methods for enriching for target DNA sequences containing at least a partial coding region for at least one specified activity in a DNA sample, as defined by amended claims 1, 27 and 28. Instead, the '485 patent describes *combinatorial* gene expression libraries constructed by stochastic genetic manipulation from genetic material of organisms that are known or are prospective sources of drugs. For example, the '485 patent teaches that individual genes from different species can be concatenated in a way that is predetermined so as to produce a potentially novel, but non-naturally occurring pathway. In addition, the '485 patent teaches cloning genes, at least one of which is a known gene, from several different organisms into a single host cell, with the result being the formation of potentially new pathways. For example, in the '485 patent, a single host cell might contain gene A, which is a known gene, from organism A, gene B from organism B and gene C from organism C, thereby producing a novel metabolic pathway encoded by genes combined from various organisms.

Applicants provide extrinsic evidence in support of the meaning of "combinatorial" as used in the '485 teaching to distinguish from Applicants' teaching and claims directed to naturally occurring DNA encoding activities of interest, including operons. Exhibit B is a print out from an internet site which includes a description of Neugenesis' combinatorial biology technology, which creates "combinatorial panels of heavy and light chains of a heteromeric

protein and to build libraries of diverse, new, fully assembled proteins. Variants of each subunit gene are generated within the host by Neugenesis' proprietary technology." (http://www.neugenesis.com/) Clearly, Applicant's claims are not directed to combinatorial approaches to identifying enzyme activities encoded by naturally occurring gene clusters, since Applicant is not manipulating the DNA to generate variants.

Exhibit C is a printout from the internet site of the Koide Group, from University of Pittsburgh (http://www.pitt.edu/~sparano/group/). As you will note, the study of Natural Products is separate and distinct from the study of Combinatorial Libraries. Exhibit D provides a glossary of terms used in Medicinal Chemistry. On page 4, the term combinatorial synthesis is described as "...combining sets of building blocks" e.g., ligating together individual genes of a gene cluster.

Applicants submit that all of this evidence supports Applicants' prior arguments distinguishing Applicants' claimed invention from the combinatorial methods described in the '485 patent. Accordingly, Applicant respectfully submits that Thompson fails to teach each and every element of the claimed invention as would be required to support a rejection under 35 U.S.C. §102(e) and reconsideration and withdrawal of the rejection are respectfully requested.

The Rejection under 35 U.S.C. § 103

Applicants respectfully traverse the rejection of claims 1-6, 8-19, and 24-26 under 35 U.S.C. § 103 as allegedly being unpatentable over the '485 patent as applied above and in view of Short (U.S. Patent No. 5,958,672; hereinafter "Short"). The deficiencies of the

'485 patent described above for disclosing the invention methods apply equally and are incorporated here.

In addition, with regard to Short, Applicants submit herewith a Declaration under 37 C.F.R. §1.132 executed by Jay M. Short, President, Chief Executive Officer and Chief Technology Officer of Diversa Corporation declaring that the present application and U.S. Patent No. 5,958,672 are commonly owned by Diversa Corporation, and were co-owned at the time of the respective inventions, as evidenced by Assignments recorded at the U.S. Patent and Trademark Office. In view of the this Declaration, Applicants submit that U.S. Patent No. 5,958,672 is not available as a reference under 35 U.S.C. § 102(e)/103 as amended by H.R. 2215 (Technical Amendment Act). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 over the combined disclosures of Thompson and Short.

The Rejection under 35 U.S.C. § 112, Second Paragraph

Applicant respectfully traverses the rejection of claims 1-6, 8-19, and 21-28 under 35 U.S.C. § 112, Second Paragraph, as allegedly being indefinite. With regard to claims 1, 27 and 28, the Examiner asserts that the phrase "a detectable label" as used therein lacks clarity because the Specification teaches how to use a detectable label including a "ligand" and a "specific binding partner" for selection but does not address how to use the label in a subsequent screening step if one binding partner is within the encapsulated microenvironment and not accessible for binding to its binding partner (Office Action, page 6).

However, according to the language of the present claims the "detectable label" is required to be "co-encapsulated" with the target DNA and the DNA probes comprising the detectable label. Thus, even in the case questioned by the Examiner where the detectable label

comprises a ligand and a specific binding partner the two parts of the label are both contained within the micro-environment and can readily interact to generate a detectable signal.

Moreover, Applicants teach that one of the pair of ligand and specific binding partner can be generated within the microenvironment through interaction of the components that are incorporated therein. For example, paragraphs [0179] and [0180] describe various ligand-receptor interactions that can be disrupted by a compound generated by a cell co-encapsulated with the receptor-ligand combination. Such a disruption is can be detected by a change in fluorescence before and after the disruption. In addition, "marker genes," such as those encoding a fluorescent protein can be engineered into a host cell. Modification of the expression level of the "marker gene" by a compound or molecule produced by the cell within the microenvironment is also detected by "screening" as the term is used in the claims at issue.

Thus, Applicants respectfully submit that the description of ligand-receptor pairs as useful for "selecting" molecules of interest (referred to by the Examiner) is not the only embodiment of the invention described in the Specification wherein a "ligand" and a "specific binding partner" are paired to function as a "detectable marker." Moreover, Applicants respectfully submit that the Specification describes how the pair can function as a "detectable marker" while co-encapsulated within a "microenvironment," such as a liposome. Accordingly, Applicants submit that in view of the description of the invention in the Specification, claims 1-6, 8-19, and 21-28 meet all requirements under 35 U.S.C. § 112, Second Paragraph, and reconsideration and withdrawal of the rejection are respectfully requested.

With regard to the rejection of claim 24 due to alleged lack of antecedent basis for the term "the detectable marker" in line 1, Applicants have amended claim 24 to substitute "the detectable label" for the term at issue. Antecedent basis for the term "the detectable label" is provided in claim 1, upon which claim 24 is dependent. Thus, Applicants submit that grounds

for the rejection of claim 24 for lack of clarity under 35 U.S.C. § 112, Second Paragraph, are overcome and reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above amendments and remarks, Applicants respectfully submit that all rejections are now overcome and allowance of the pending claims is respectfully requested. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosures: Exhibit A– Substitute Formal Drawings
Exhibit B -- printout
Exhibit C – printout
Exhibit D – glossary
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